**UNITED STATES DEPARTMENT OF COMMERCE**
**Patent and Trademark Office**

Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, DC 20231

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
|---|---|---|---|
| 08/225,478 | 04/08/94 | KOHN | D |

| EXAMINER | |
|---|---|
| STANTON, D | 1628 |
| ART UNIT | PAPER NUMBER |

HM31/0820

RAYMOND J LILLIE
CARELLA, BYRNE, BAIN, GILFILLAN, CECCHI,
STEWART & OLSTEIN
6 BECKER FARM RD.
ROSELAND NJ 07068

DATE MAILED: 08/20/98

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**



☆U.S.GOVERNMENT PRINTING OFFICE 1995-319-826

| Office Action Summary | Application No. 08/225,478 | Applicant(s) Kohn et al. |
|---|---|---|
| | Examiner Brian R. Stanton | Group Art Unit 1632 |

☒ Responsive to communication(s) filed on *Jun 9, 1998* .

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three (3)* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

**Disposition of Claims**

☒ Claim(s) *1-15 and 21-26* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-15 and 21-26* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

**Application Papers**

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

*--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---*

The response filed 6/9/98 (Paper No. 35) has been entered. Claims 16-20 have been canceled. Claims 1-15 and 21-26 remain pending in the instant Application. Applicant's arguments filed 6/9/98 (Paper No. 15) have been fully considered but they are not persuasive.

***Claim Rejections - 35 USC § 112***

Claims 1-5 and 16-22 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited to methods of treating severe combined immunodeficiency syndrome using therapeutic gene transfer to autologous CD34+ cell obtained from cord blood cells wherein said cells have been genetically engineered with a nucleic acid encoding adenosine deaminase (ADA) and further wherein said cord blood cells are administered to a patient such that said ADA encoding nucleic acid is expressed in an amount sufficient to provide a therapeutic effect, does not reasonably provide enablement for the treatment of any and all diseases with any and all cells and nucleic acids. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. This rejection is maintained for reasons of record advanced in the preceding Office Action mailed 5/28/97 (Paper No. 29). Applicant's arguments filed 6/9/98 (Paper No. 15) have been fully considered but they are not persuasive.

Applicant argues that the Kohn et al. 1995 paper, while indicating that further work may be required to express various genes *in vivo* does not mean that such work would have represented undue experimentation. Applicant continues by urging that since they have demonstrated that the instant invention may be used in combination with the human ADA gene, one skilled in the art would have reasonably expected that other genes may be used in combination with what is claimed. Applicant then states that the Examiner has not provided any evidence, other than speculative statements, that would indicate that other genes could not be expressed in accordance with the claimed methods.

In response, it is first noted that the claims under instant specification are limited to "expressing a therapeutic agent" in a human, and although no concordant process step associated

with such is recited in the claims, the specification must enable not only the preparation of transformed cells, but the use of the cells to deliver a therapeutic agent. Further, the claimed invention as pending is not enabled since such a concordant process step is not recited. Applicants arguments fail to obviate the necessity for such a recitation.

Second, applicant has not tendered any evidence or argument to support that undue experimentation would not have been required to have expressed therapeutic agents in humans. While applicant asserts that the Examiner has not provided any evidence that such would have been undue, such has indeed been advanced by reference to not only Kohn et al, 1995, but also to the "Report and Recommendations of the Panel to Assess the NIH Investment in Research on Gene Therapy" that took place on December 7, 1995, that was cited in the prior Office Action mailed 2/3/98. Thus, given that applicant has not provided any rebuttal evidence that indicates that the instant disclosure overcomes the limitations of the art as exemplified by both the cited prior art references, applicant has failed to obviate the *prima facie* case of non-enablement for the full scope of the claims, that has been established and is of record.

Third, it is noted that the issue at hand is not simply that transformed cells could be prepared, but the cells, once transduced, would also have been able to effect the therapeutic expression of an agent in a human. While the claims have been amended to delete reference to garnering a therapeutic effect, when the claims (e.g. claim 1) are read in light of the specification, such an effect is the only use set forth for the claimed expression and therefore must be enabled.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-15 and 21-26 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson et al., 1992, Moritz et al., 1993 and Kohn et al., 1992 (all previously cited), the preceding combination in view of either or Boyse et al., 1993 or Moore et al., 1993 for reasons of record advanced in the preceding Office Action mailed 2/3/98 (Paper No. 33). Applicant's arguments filed 6/9/98 (Paper No. 15) have been fully considered but they are not persuasive.

Applicant argues that they were the first to demonstrate what is claimed in regard to the use of cord blood for genetically engineering CD34+ cells that can be returned to a patient. However, this point is not disputed since no rejection is standing under 35 USC 102. However, the issue at hand is that in view of the combination of cited references, the claimed invention would have obvious to one of ordinary skill in the art at the time of the invention.

Applicant argues that none of the severally cited references disclose what is claimed. However, the instant rejection has been advanced in view of the combination of references, not any individual reference in and of itself and one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant argues that the combination of cited prior art, at best, provides "sheer speculation" that such methods as claimed by applicant could be effected (see Paper No. 35 at page 4, second paragraph). However, applicant has not provided any reason or support for this assertion nor has applicant presented any rationale as to why the artisan would not have had a reasonable expectation of success in the practice of the invention as would have been suggested

by the prior art of record. In the absence of such reasoning or evidence, applicant's assertion of "sheer speculation" is insufficient to rebut the established *prima facie* case of obviousness.

No claim is allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian R. Stanton whose telephone number is (703) 308-2801. The examiner can normally be reached on Monday to Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jasemine Chambers, can be reached on (703) 308-2035. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Brian R. Stanton, Ph.D.
August 18, 1998

BRIAN R. STANTON
PRIMARY EXAMINER
GROUP 1800
1600